Transplantation of genetically corrected iPSC-microglia for the treatment of Sanfilippo Syndrome (MPSIIIA)

Grant Award Details

Transplantation of genetically corrected iPSC-microglia for the treatment of Sanfilippo Syndrome (MPSIIIA)

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13077

Investigator:

Name:	Mathew Blurton-Jones
Institution:	University of California, Irvine
Type:	PI

Award Value: $1,199,922

Status: Pre-Active

Grant Application Details

Application Title: Transplantation of genetically corrected iPSC-microglia for the treatment of Sanfilippo Syndrome (MPSIIIA)

Public Abstract:

Research Objective

This research will discover whether transplantation of stem cell-derived microglia can be used to treat Sanfilippo syndrome, a devastating and currently untreatable childhood neurological disease.

Impact

If successful, this research will identify a promising new therapeutic approach for Sanfilippo Syndrome and provide the first evidence that stem cell derived microglia could be used therapeutically.

Major Proposed Activities

- We will use CRISPR technology to correct disease-associated mutations in the SGSG gene in human stem cell lines that we have generated from patients with Sanfilippo Syndrome (MPSIIIA).
- Patient-derived and CRISPR corrected stem cells will be differentiated into microglia, an immune cell type that is dysfunctional in MPSIIIA, and then transplanted into a mouse model of this disease.
- Three months after transplantation we will examine MPSIIIA-associated neuropathologies to determine whether transplantation of genetically-corrected microglia has reduced disease pathology.
- Microglia that are engineered to produce and secrete higher levels of the missing SGSH enzyme may provide additional long term benefits. We will therefore test the efficacy of this additional approach
- 6-months after transplantation we will examine neuropathologies to determine whether SGSH secreting microglia improve cognitive function and provide additional long-term benefits in MPSIIIA mice.
- Analysis of biomarkers, neuropathology, cognitive function, and RNA sequencing of brain cells will be used to determine the optimal approach to reduce MPSIIIA cognitive deficits and neuropathology

Statement of Benefit to California:

Sanfilippo syndrome (MPSIIIA) is a devastating pediatric neurological disease that effects families of all ethnicities and race including many Californians. Sadly, currently approved therapies provide little benefit. Our research aims to develop a new stem cell-based therapy for MPSIIIA that uses microglia, the immune cell of the brain. If successful, this new approach could also potentially be developed to treat many other neurological diseases that are highly prevalent in California.
